REMARKS

This is in response to the Office Action that was mailed on June 4, 2004. The requirement for restriction amongst plasminogen-, endostatin-, VEGF-, and KDR/FLK-derived peptides having been made final, claims 1, 7, and 10 are amended and claims 3-5 and 9 have been cancelled, without prejudice to their reassertion in this or a continuing application. Claims 1 is amended to recite a proline residue feature based upon disclosure in the paragraph bridging pages 6-7 of the specification. New claim 29 is based upon the same disclosure. Claims 19, 20, 22, 23, 17, and 28 are amended to clarify that "undesired" angiogenesis is tumor angiogenesis. Note *e.g.* the Background of the Invention section of the specification ("Many molecules that inhibit tumor angiogenesis have been shown to inhibit tumor growth....") Claims 19, 20, 22, 23, 27, and 28 are amended to delete the term "undesired". Claim 10 and the specification are amended to conform the sequence identifiers with preferred practice. No new matter is introduced by this Amendment. Claims 1, 2, 6-8, 10, 13-16, 19, 20, 22, 23, and 25-29 are in the application.

RESTRICTION. Restriction was required, and made FINAL, amongst plasminogen-derived peptides, endostatin-derived peptides, VEGF-derived peptides, and KDR/FLK-derived peptides and their uses, as disclosed and claimed herein.

Accordingly, all but the elected endostatin-derived peptides and their uses have been cancelled from the present application.

ELECTION OF SPECIES. In response to an election of species, Applicants had elected the species of invention that involves SEQ ID NO:30. Claims 1, 2, 6-8, 10, 13-16, 19, 20, 22, 23, and 25-29 all read on or relate to the elected species.

Claims 19, 22, 27, and 28 were rejected under the first paragraph of 35 U.S.C. §112 as allegedly failing to comply with the written description requirement. This rejection is respectfully traversed. Reconsideration and withdrawal of this ground of rejection are earnestly solicited.

Applicants contend that the specification in fact very well describes the presently claimed invention. To assist the Examiner's reading of the specification, the following disclosure in the specification is pointed out as exemplary of the description of the invention therein. The Examiner might note for instance: page 4, lines 12-15; page 6, lines 3-6; page 6, lines 6-10 (how to make); and page 7, line 19 through page 8, line 11 (how to use). For instance, "Administration of the peptides for anti-tumor treatment can be by any route .... subcutaneous administration is especially effective when anti-metastatic activity is desired ....". Page 7, lines 27-31.

Moreover, the claims in question have been amended to recite (only) methods of treating undesired (that is, tumor) angiogenesis.

At the top of page 7 of the Office Action, the Examiner alleges that there is no "recognized model (identified as useful) being treated according to methods of preventing or treating a subject for the conditions being claimed". While it is not clear that this is relevant to a written description rejection, enclosed herewith is a copy of a journal article showing such a model, namely, Ueda et al., "Effects of an anti-angiogenic agent, TNP-470, on the growth of oral squamous cell carcinomas", *Oral Oncol.*, 35 (6):554-560 (1999). The Examiner's attention is also directed to the following articles: Offodile et al., "Regression of metastatic breast cancer in a patient treated with the anti-angiogenic drug TNP-470", *Tumori*, 85(1):51-53 (1999); and Cobleigh et al., "A phase I/II dose-escalation trial of bevacizumab in previously treated metastatic breast cancer", *Semin Oncol*, 30(5 Suppl 16):117-124 (2003).

It is clear that the invention of the present claims is fully described – in writing – in the specification.

Claims 19, 22, 27, and 28 were rejected under the second paragraph of 35 U.S.C. §112 as failing to define the invention properly. The Examiner maintained that it was not clear what was meant by the phrase "undesired angiogenesis", to the extent that it related to something other than treating a tumor. The claims have been amended to delete the qualitative term "undesired" and to clarify the tumor-

related nature of the angiogenesis involved. It is respectfully submitted that the claims in their present form satisfy the requirements of the statute.

Claims 1, 2, 6-8, 13, 14, 25, and 26 were rejected under 35 U.S.C. §102(b) as being anticipated by *Cell*, Vol. 88, pp. 277-285 (O'Reilly). The rejection is respectfully traversed.

The emphasized portion of the Examiner's allegation that "the prior art discloses SEQ ID NO:30 (i.e., ***residues 7-19 which are*** QPVLHLVALNTPL) as directed to claim 25" (emphasis supplied) is not understood. Explanation is respectfully requested. In any case, the Examiner mis-characterizes the O'Reilly paper. O'Reilly describes an angiogenesis inhibitor, called "endostatin", which is a 20 kDa, C-terminal fragment of collagen XVIII (see "Summary" at p. 277). A 20 kDa peptide is expected to have a length of 181 amino acids (at an average molecular weight per residue of 110). O'Reilly does not describe anti-angiogenic activity of any shorter peptide.

Furthermore, such shorter peptide as is noted by O'Reilly is mentioned as an N-terminal fragment that was sequenced to identify the endostatin protein. The peptide that is actually described has the sequence "HTHQDFQPVLHLVALNTPLS". Manifestly, this peptide does not contain "a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide", as required by claims 1, 2, 6-8, 10, 13-16, 19, 20, 22, 23, and 25-28 herein. The

peptide described in the O'Reilly reference does not contain "two proline residues each being located penultimate to a terminus of the peptide", as required by claim 29 herein. Withdrawal of the rejection over O'Reilly is respectfully solicited.

If there are any remaining issues, the Examiner is invited to telephone Richard Gallagher (Reg. No. 28,781) at (703) 205-8008.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to debit Deposit Account No. 02-2448 for any additional fee required under 37 C.F.R. §1.16 or §1.17, particularly extension of time fees, or to credit said Deposit Account for any overpayment of fees.

Respectfully submitted,
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Enclosed:
Ueda et al., *Oral Oncol.*, 35(6):554-560 (1999).